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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/675,020	09/29/2003	Stephen Donovan	17510DIV1 (BOT)	4829

7590 02/08/2007

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EXAMINER	
FORD, VANESSA L	
ART UNIT	PAPER NUMBER
1645	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/08/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/675,020	DONOVAN, STEPHEN	
	Examiner	Art Unit	
	Vanessa L. Ford	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 November 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-21 and 36-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-21 and 36-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

FINAL ACTION

1. This action is responsive to Applicant's amendment and response filed November 8, 2006 is acknowledged. Claims 1-15 and 22-35 have been cancelled. Claims 16-21 and 36-44 are pending and under examination in this office action.

Rejection Withdrawn

2. In view of Applicant's amendment and remarks the rejection of claims 16-21 and 36-44 under 35 U.S.C. 103(a) pages 2-5, paragraph 4 of the previous Office action has been withdrawn.

New Grounds of Rejection Necessitated by Amendment

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

3. Claims 16-17, 20-21, 39-40 and 44 are rejected under 35 U.S.C. 102(a) as anticipated by Graham *(U.S. Patent No. 6,939,852 B2 published September 6, 2005).*

Claims 16-17, 20-21, 39-40 and 44 are drawn to a transdermal patch comprising a pharmaceutical composition which comprises a stabilized botulinum toxin provided in a dried state and an enhancing agent that is mixable with the stabilized botulinum toxin provided in a dried state and facilitates transdermal administration of a botulinum toxin in a bioactive form to a subdermal target site of a human patient without being

administered to the patient's circulatory system; and an adhesive disposed to one side of the transdermal patch to irremovably secure the patch in the patient's skin.

Graham teaches a pharmaceutical composition comprising botulinum toxin A incorporated into a polymetric matrix of a suitable carrier and formed into a adhesive patch for use in conjunction with a skin permeation enhancer such as DMS or Azone (column 4). Graham teaches that the botulinum toxin used in the invention dried or lyophilized (column 4). Claim limitations such as "facilitates transdermal administration of a botulinum toxin in a bioactive form to a subdermal target site of a human patient without being administered to the patient's circulatory system", wherein the botulinum in the dried state is provided in a dry state in plurality of wells, each of the wells covered by a membrane that is dissolvable with a fluid and wherein the enhancing agent mixes with the botulinum toxin as the membrane over a well dissolves so that the absorption of the botulinum toxin is enhanced, wherein the transdermal patch of claim 39 wherein less than 25% of the administered botulinum toxin permeates into a blood vessel" would be inherent in the teachings of the prior art since the patch is used for transdermal delivery. Graham anticipates the claimed invention.

Since the Office does not have the facilities for examining and comparing applicant's transdermal patch with the transdermal patch of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the transdermal patch of the prior art does not possess the same material structural and functional characteristics of the claimed

transdermal patch). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 18 and 19 are rejected under 35 U.S.C. 103(a) as unpatentable over Graham *(U.S. Patent No. 6,939,852 B2 published September 6, 2005)* in view of Yuzhakov et al *(U.S. Patent No. 6,939,852 B2 published September 6, 2005).*

Claims 18 and 19 are drawn to the transdermal patch of claims 16 further comprising a plurality of needles extending from one side of the patch that is applied to the skin, wherein the needles extend from the patch to project through the stratum corneum of the skin without rupturing a blood vessel.

The teachings of Graham has been described previously.

Graham does not teach the claim 18 which is drawn to the transdermal patch of claim 16 further comprising a plurality of needles extending from one side of the patch that is applied to the skin, wherein the needles extend from the patch to project through the stratum corneum of the skin without rupturing a blood vessel.

Yuzhakov et al teach that the transdermal patch contains a microneedle array (column 3). Yuzhakov et al teach that the invention is projected or penetrates the stratum corneum (column 3).

It would be *prima facie* obvious at the time the invention was made to modify the transdermal patch as taught by Graham to include the needle array as taught by Yuzhakov et al because Yuzhakov et al teach that the invention is projected or penetrates the stratum corneum to transfer actives or skin support structures to the epidermis (column 3). It would be expected barring evidence to the contrary, that incorporating needle array as taught by Yuzhakov et al into transdermal patches of Graham would be an effective way to facilitate the delivery of active agents such as botulinum toxin to a subdermal target of a patient.

5. Claims 36-38 and 41-43 are rejected under 35 U.S.C. 103(a) as unpatentable over Graham *(U.S. Patent No. 6,939,852 B2 published September 6, 2005)* in view of Cevc *(U.S. Patent No.6,165,500 published December 26, 2000)*.

Claims 36-38 and 41-43 are drawn to the transdermal patch of claim 16 wherein the enhancing agent comprises 1 part water, 1 part ethanol and 2 part polyethylene glycol, wherein the transdermal patch of claim 36 is 90% ethanol and the transdermal patch of claim 16, wherein the enhancing agent comprises 1 part of 10% transfersomes and 0,9 part of a buffer.

The teachings of Graham has been described previously.

Graham does not teach the limitations of claims 36-38 and 41-43 which are wherein the transdermal patch of claim 16 or 39, wherein the enhancing agent comprise 1 part water, 1 part ethanol, and 1 part polyethylene glycol", the transdermal patch of claim 16 or 39, wherein the enhancing agent comprises 1 part of 10% transfersomes and 0.9 part of a buffer" and "the transdermal patch of claim 36 or 39 wherein the ethanol is 90% ethanol".

Cevc teaches that solvents such as ethanol (enhancing agents) can be used to induce or increase the carrier system's capacity to form edges, protrusions or relatively strongly curved surfaces; this property also manifests itself in the capability to induce pores in lipid structures, such as membranes, or even provoke a solubilization (lysis) in the higher concentrations ranges (columns 7-8). Cevc teaches that the transfersome compositions of the invention can be introduced not only to a permeability barrier such as the skin (column 4, 66-67 and column 5, lines 1-4). Cevc teaches compositions that comprise transfersomes ranging in concentration from 0.1 to 99% of the total composition (column 4, lines 47-56) Cevc teaches the use of edge active substances used in the transfersomes such as polyethylene glycol (columns 7-9). Ceve teaches buffer such as Hepes (column 55). Cevc teaches that the ethanol use to in the claimed invention is absolute ethanol (columns 55-56), therefore the ethanol taught by the prior art teaches the claim limitation "wherein the ethanol is 90% ethanol".

Regarding the specific concentrations listed in the instant claims,

> MPEP 2144.05 states, "Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be *prima facie* obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); see also *Peterson*, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); *In re Hoeschele*, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.). For more recent cases applying this principle, see *Merck & Co. Inc. v. Biocraft Laboratories Inc.*, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), *cert. denied*, 493 U.S. 975 (1989); *In re Kulling*, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997)."

It would be *prima facie* obvious at the time the invention was made to modify the transderam patch as taught by Graham to be incorporated into the transfersomes as taught by Cevc because Cevc teaches compositions that comprise transfersomes ranging in concentration from 0.1 to 99% of the total composition (column 4, lines 47-56), the use of edge active substances used in the transfersomes such as polyethylene glycol (columns 7-9) and the use of buffers such as Hepes (column 55). Cevc also teaches that the ethanol use to in the claimed invention is absolute ethanol (columns 55-56), therefore the ethanol taught by the prior art teaches the claim limitation "wherein the ethanol is 90% ethanol". It would be expected barring evidence to the contrary, that

incorporating transfersomes into transdermal patches would be an effective way to facilitate the delivery of active agents such as botulinum toxin to a subdermal target of a patient.

6. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Status of Claims

7. No claims allowed.

Conclusion

8. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 872-9306.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (571) 272-0857. The examiner can normally be reached on Monday – Thursday from 9:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffery Siew, can be reached at (571) 272-0787

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov./>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

VLF

Vanessa L. Ford
Biotechnology Patent Examiner
January 16, 2007

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER